Influence of Sex on the Changes in Regional Fat and Skeletal Muscle Mass in Response to Exercise Training in Adolescents with Obesity

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Abstract

Background: We retrospectively examined the sex differences in the changes in (1) total fat, total and regional subcutaneous adipose tissue (SAT), visceral fat, and intermuscular fat and (2) total and regional skeletal muscle distribution in response to aerobic exercise (AE) or resistance exercise (RE) in adolescents with obesity.

Methods: Twenty-eight boys and 27 girls with obesity (BMI $\geq$ 95th percentile, 12–18 years) were randomly assigned to 3-month interventions (180 minutes per week) of AE or RE. Changes in total and regional fat and skeletal muscle distribution were assessed by a whole-body magnetic resonance imaging.

Results: After controlling for corresponding baseline values, age, and race, changes in body weight, BMI, BMI z-score, and waist circumference were similar between exercise groups ($p > 0.05$) and sexes ($p > 0.05$). There were no sex or exercise group differences in the reductions in total fat, total SAT, visceral fat, or intermuscular fat. With AE, boys had greater ($p < 0.05$) reductions in abdominal SAT as compared with girls. With RE, boys had greater ($p < 0.05$) increases in total, upper body, and abdominal skeletal muscle as compared with girls. Independent of exercise modality, the improvement in $\text{VO}_{2\text{max}}$ was greater ($p < 0.05$) in boys than in girls. Independent of sex, the increase in muscular strength index was higher ($p < 0.05$) in the RE vs. AE group.

Conclusion: With the exception of abdominal SAT, there were no sex or exercise treatment differences in the reductions in total and regional fat. In response to RE, the increases in total and regional skeletal muscle were significantly greater in boys than in girls.

Keywords: adipose tissue; adolescents; childhood obesity; exercise; skeletal muscle

Background

Although it is well demonstrated that regular exercise is associated with significant reductions in total adiposity, it is unclear whether sex influences the effects of regular exercise on regional adipose tissue (AT) and skeletal muscle distribution in youth. In adults, studies have shown that during weight loss, men with obesity lose significantly more visceral fat than women with obesity.^{1–5} Specifically, a meta-analysis by Vissers et al.⁶ reported that in response to aerobic exercise (AE) (e.g., without hypocaloric diet), men demonstrated a greater reduction in visceral fat than women. However, as the magnitude of fat loss is related to baseline values, it is reasonable to believe that men are expected to lose more visceral fat with inter-

ventions as they have more visceral fat than women.¹ Alternatively, sex differences in catecholamine-stimulated lipolysis or hormone levels⁷ may explain the differences in regional fat change between men and women. As marked changes in body composition and fat distribution emerge during puberty and maturation,⁸ it is unclear whether sex difference in fat and skeletal muscle distribution with exercise training are also present during adolescence.

In a recent meta-analysis, Vissers et al.⁹ have reported that regular exercise with and without caloric restriction is more effective than caloric restriction alone to reduce visceral fat in children and adolescents with obesity. Most included studies in this meta-analysis⁹ employed AE as a strategy for the treatment of obesity in youth. Recently, resistance exercise (RE) has become a popular

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mode of exercise for youth with obesity as RE, as incorporating single- and multijoint whole-body exercise has been shown to be effective in increasing fat-free mass, muscular strength and endurance, and reducing percentage body fat in youth.^{10–12}

Therefore, we examined the sex and exercise type differences in the changes in (1) total fat, whole-body and regional subcutaneous adipose tissue (SAT), visceral fat, and intermuscular fat and (2) total and regional skeletal muscle distribution in response to a 3-month AE or RE intervention in adolescents with obesity.

Methods

Participants

This study is a secondary analysis of 55 boys and girls with obesity who were part of two previously published trials^{13,14} and had complete baseline and follow-up whole-body magnetic resonance imaging (MRI). Some of the data have been published previously.^{13,14} For both trials, participants were recruited through newspaper advertisements, flyers, and posters in the greater Pittsburgh area. Inclusion criteria for both trials were as follows: 12–18 years of age, Tanner stages III–V, nondiabetic, nonsmokers, and sedentary (no structured physical activity in the 3 months before the study). Exclusion criteria included chronic diseases (e.g., asthma, syndromic obesity, psychiatric disorder, diabetes, and polycystic ovary syndrome), medications that may result in a change in glucose metabolism or body composition, and significant weight change ($\text{BMI} > 2\text{--}3 \text{ kg/m}^2$) in the 3 months before the study. All participants were given a thorough physical examination by a nurse practitioner and routine hematologic and biochemical tests at the Pediatric Clinical and Translational Research Center at Children's Hospital of Pittsburgh. The investigation was approved by the University of Pittsburgh Institutional Review Board and the research procedures were conducted in accordance with the Declaration of Helsinki. Parental informed consent and child assent were obtained from all participants before participation.

Intervention Regimen

A detailed description of the exercise interventions was reported previously.^{13,14} In brief, participants in the AE group used either treadmills, ellipticals, or stationary bikes at 50%–75% of $\text{VO}_{2\text{peak}}$, three times per week (60 minutes per session), for 3 months. Participants in the resistance group used weight machines and performed a series of 10 whole body REs (1–2 sets, 8–12 repetitions), three times per week (60 minutes per session), for 3 months. Exercise attendance was >95% in all groups. All participants were asked to follow a weight maintenance diet (55%–60% carbohydrate, 15%–20% protein, and 20%–25% fat) during the intervention period to be able to assess that any changes in body composition are consequent to the effects of regular exercise alone and not from caloric restriction.

Anthropometric Measurements

Body weight was measured to the nearest 0.1 kg and height was measured to the nearest 0.1 cm. Waist circumference was measured at the level of the last rib and the average of two measures was used.

Whole-Body MRI

Total and regional AT and skeletal muscle distribution were examined using a 3.0 Tesla MR scanner (Siemens, Magnetom TIM Trio, Germany) at the University of Pittsburgh Magnetic Resonance Research Center. As shown previously,^{13,14} the participants lay in the magnet in a prone position with their arms placed straight overhead. Using the L4–L5 as the point of origin, transverse images (10 mm image thickness) were obtained every 50 mm to the hand and foot. Three series of 7 images (e.g., 7 images per series) were obtained for the lower body and 3 series of 7 images were obtained for the upper body, resulting in a total of ~41 equidistant images for each subject. Once acquired, the MRI data were transferred electronically to a stand-alone computer for analysis using specially designed image analysis software (TomoVision, Montreal, Canada), the procedures for which are fully described elsewhere.^{15,16}

Determination of Regional AT and Skeletal Muscle Mass

The methods used to segment and calculate the AT and skeletal muscle areas are fully described elsewhere.^{15,16} Whole-body total fat (subcutaneous + visceral + intrathoracic + intrapelvic + interstitial AT), SAT, intermuscular fat (AT area beneath the fascia lata surrounding skeletal muscle and AT area between muscle bundles), skeletal muscle (skeletal muscle – intermuscular fat), and lean tissue (skeletal muscle + organ + bone + connective tissue) volumes were determined using all ~41 images. As shown by Kuk and Ross,¹⁷ the image at 5 cm below L4–L5 was used to divide the upper body and lower body. Total visceral fat and abdominal SAT and skeletal muscle volumes were calculated using the five images extending from 5 cm below to 15 cm above L4–L5. AT and skeletal muscle volume were converted to mass units (kg) by multiplying the volumes by the assumed constant density for AT (0.92 kg/L) and skeletal muscle (1.04 kg/L).¹⁸

Fitness Measurements

Cardiorespiratory fitness was determined using a graded treadmill test with the use of standard open-circuit spirometry techniques (AEI Technologies, Pittsburgh, PA) until volitional fatigue.^{13,14} $\text{VO}_{2\text{max}}$ was attained when at least two of the following three criteria were achieved: (1) a change in VO_2 of <2.1 mL/(kg·min) with increasing exercise intensity at near-maximum higher treadmill stages, (2) a respiratory exchange ratio in excess of 1.05, and/or (3) heart rate >90% of the age-predicted maximum (220-age).

One-repetition maximum (1-RM) leg press and 1-RM chest press were measured using weight stack equipment

(Life Fitness, Schiller Park, IL) to evaluate lower body and upper body strength, respectively. Based on the American College of Sports Medicine's guidelines, proper lifting techniques and testing procedures were given to participants before the test.¹⁹ After the collection of upper and lower body strength data, whole-body muscle strength index was calculated by adding chest press 1-RM (kg) with leg press 1-RM (kg) and dividing the total by the subject's body weight (kg).²⁰

Statistical Analysis

Differences in the baseline characteristics by sex and exercise type were examined using analysis of variance. Change scores in total and regional AT and skeletal muscle mass with exercise training were assessed using repeated measures general linear modeling, with adjustment for age, race, and corresponding baseline values with least squared adjusted means *post hoc* tests. All analyses were performed with

commercially available software (SAS, version 9.4). *p* Values of <0.05 were accepted to indicate statistical significance.

Results

Baseline Characteristics

Baseline characteristics stratified by sex and exercise group are given in Table 1. There were minimal differences in total or regional fat by sex or exercise group, whereas boys consistently had higher total and regional skeletal muscle mass, and lean tissue mass than girls ($p < 0.05$).

Influence of Sex on the Changes in Fitness

After controlling for baseline values, age, and race, the improvement in $\text{VO}_{2\text{max}}$ was greater ($p < 0.05$) in boys than in girls with both exercise modalities (Fig. 1A). In response to RE, the increase in muscular strength index was significantly greater in boys than in girls (Fig. 1B). Independent of

Table 1. Subject Characteristics at Baseline

Variable	AE		RE	
	Boys	Girls	Boys	Girls
<i>n</i>	14	13	14	14
Age (years)	15.1 ± 1.7	14.9 ± 1.9	14.8 ± 1.5	14.8 ± 1.7
Weight (kg)	107.7 ± 17.1*	91.7 ± 16.8	98.7 ± 11.2	96.2 ± 16.5
BMI (kg/m ²)	36.8 ± 5.6*	33.4 ± 4.1	34.5 ± 2.5	36.1 ± 4.0
BMI z-score	2.5 ± 0.3*	2.1 ± 0.3	2.4 ± 0.2	2.3 ± 0.3
Waist (cm)	114.6 ± 11.4	108.4 ± 11.5	109.0 ± 8.9	113.4 ± 11.2
Total AT (kg)	46.9 ± 11.6	44.2 ± 11.6	43.4 ± 9.0	49.9 ± 12.2
Total SAT (kg)	39.9 ± 10.4	38.7 ± 10.5	37.6 ± 8.3	43.2 ± 10.1
Upper body SAT (kg)	19.9 ± 6.3	18.3 ± 5.8	18.1 ± 5.0	21.6 ± 5.3
Lower body SAT (kg)	20.0 ± 4.9	20.4 ± 5.5	19.5 ± 4.9	21.6 ± 5.2
Abdominal SAT (kg)	7.9 ± 2.5	6.9 ± 2.1	6.7 ± 1.8	8.0 ± 2.0
Visceral fat (kg)	1.5 ± 0.5*	0.9 ± 0.3	1.4 ± 0.6	1.2 ± 0.6
Intermuscular fat (kg)	4.1 ± 1.2	3.4 ± 1.3	3.3 ± 0.7	3.9 ± 1.6
Total SM (kg)	31.0 ± 4.8*	23.6 ± 4.1	27.2 ± 4.0* [†]	22.9 ± 2.9
Upper body SM (kg)	12.6 ± 2.1*	9.3 ± 2.0	10.9 ± 1.6* [†]	9.0 ± 1.1
Lower body SM (kg)	18.4 ± 2.9*	14.3 ± 2.3	16.3 ± 2.6* [†]	13.9 ± 1.9
Abdominal SM (kg)	3.4 ± 0.5*	2.5 ± 0.5	3.0 ± 0.4* [†]	2.5 ± 0.2
SM:AT ratio	0.69 ± 0.14*	0.55 ± 0.08	0.66 ± 0.19*	0.48 ± 0.10
Lean tissue (kg)	54.0 ± 7.4*	44.2 ± 5.7	49.4 ± 6.6*	42.8 ± 5.0
$\text{VO}_{2\text{max}}$ [mL/(kg·min)]	29.7 ± 4.6	28.2 ± 4.0	30.7 ± 4.8*	24.1 ± 4.5 [†]
Muscular strength index	1.20 ± 0.17	1.04 ± 0.20	1.19 ± 0.31*	1.02 ± 0.22

Values are mean ± standard deviation.

*Significant difference from girls within group ($p < 0.05$).

[†]Significant difference from aerobic group within sex ($p < 0.05$).

AE, aerobic exercise; AT, adipose tissue; RE, resistance exercise; SAT, subcutaneous adipose tissue; SM, skeletal muscle.

FIG. 1. Changes in $VO_{2\max}$ (A) and muscular strength index (B) adjusting for age, race, and baseline values (least squared adjusted means $\pm$ standard error). *Significant difference from girls within group ($p < 0.05$). †Significant difference from aerobic group within sex ($p < 0.05$).

sex, the increase in muscular strength index was higher in the RE vs. AE group ($p < 0.01$).

Influence of Sex on the Changes in Total and Regional AT, and Skeletal Muscle Mass

After controlling for baseline values, age, and race, there were no sex or exercise group differences in the reductions

in body weight, BMI, BMI z-score, and waist circumference (Table 2). Furthermore, there were no significant sex by group interactions for the changes in total, regional fat or skeletal muscle measurements. Similarly, there were no sex or exercise group differences in the changes in total fat, total SAT, visceral fat, or intermuscular fat (Table 2; Fig. 2A, B). In response to AE, boys had greater ($p = 0.027$) reductions in abdominal SAT than girls (Fig. 2C). In response to RE,

Table 2. Absolute Changes in Total and Regional AT and SM Distribution

Variable	AE		RE	
	Boys	Girls	Boys	Girls
Weight (kg)	-1.3 ± 0.9	-1.1 ± 0.9	0.0 ± 0.8	-0.2 ± 0.8
BMI (kg/m^2)	-0.7 ± 0.3	-0.5 ± 0.3	-0.3 ± 0.3	-0.3 ± 0.3
BMI z-score	-0.04 ± 0.08	-0.08 ± 0.09	-0.04 ± 0.07	-0.04 ± 0.06
Waist (cm)	-2.2 ± 0.7	-2.4 ± 0.8	-3.0 ± 0.8	-1.0 ± 0.8
Total AT (kg)	-3.4 ± 0.8	-1.9 ± 0.8	-2.4 ± 0.8	-1.5 ± 0.8
Total SAT (kg)	-2.6 ± 0.7	-1.2 ± 0.7	-2.3 ± 0.7	-0.7 ± 0.7
Upper body SAT (kg)	-1.5 ± 0.4	-0.7 ± 0.4	-1.0 ± 0.4	-0.3 ± 0.4
Lower body SAT (kg)	-1.2 ± 0.4	-0.6 ± 0.4	-1.4 ± 0.4	-0.4 ± 0.4
Abdominal SAT (kg)	$-0.65 \pm 0.14^*$	-0.18 ± 0.15	-0.41 ± 0.14	-0.11 ± 0.14
Visceral fat (kg)	-0.14 ± 0.05	-0.25 ± 0.06	-0.18 ± 0.05	-0.16 ± 0.05
Intermuscular fat (kg)	-0.4 ± 0.2	-0.4 ± 0.2	-0.2 ± 0.2	-0.4 ± 0.2
Total SM (kg)	1.1 ± 0.4	0.1 ± 0.3	$1.7 \pm 0.3^*$	0.6 ± 0.4
Upper body SM (kg)	0.3 ± 0.2	0.0 ± 0.2	$1.0 \pm 0.2^{*,\dagger}$	$0.4 \pm 0.2^\dagger$
Lower body SM (kg)	0.8 ± 0.2	0.1 ± 0.2	0.7 ± 0.2	0.2 ± 0.2
Abdominal SM (kg)	0.13 ± 0.06	0.04 ± 0.05	$0.23 \pm 0.05^*$	0.02 ± 0.05
SM:AT ratio	0.06 ± 0.02	0.05 ± 0.02	0.07 ± 0.02	0.06 ± 0.02
Lean tissue (kg)	$1.8 \pm 0.5^*$	-0.7 ± 0.5	1.9 ± 0.5	$0.6 \pm 0.5^\dagger$

Least squared adjusted means $\pm$ standard error adjusting for age, race, and corresponding baseline values. There were no sex by treatment interactions for the changes in any of the variables.

*Significant difference from girls within group ($p < 0.05$).

†Significant difference from aerobic group within sex ($p < 0.05$).

SM, skeletal muscle.

FIG. 2. Changes in adipose tissue (A–C) and skeletal muscle (D–F) adjusting for age, race, and baseline values (least squared adjusted means $\pm$ standard error). *Significant difference from girls within group ($p < 0.05$). †Significant difference from aerobic group within sex ($p < 0.05$). SAT, subcutaneous adipose tissue; SM, skeletal muscle.

boys had significantly greater increases in total, upper body, and abdominal skeletal muscle than girls (Fig. 2D–F).

Discussion

We demonstrate that (1) with the exception of abdominal SAT, there were no significant sex or exercise treatment differences in the changes in BMI, body weight, total fat, SAT, visceral fat, or intermuscular fat mass; (2) in response to RE, but not AE, boys had significantly greater increases in total, upper body, and abdominal skeletal muscle mass than girls; and (3) independent of exercise modality, the increase in $\text{VO}_{2\text{max}}$ was significantly greater in boys than in girls.

To our knowledge, we are aware of only one randomized controlled study in pediatrics wherein the effects of exercise training on the changes in total and abdominal AT were measured with the use of whole-body MRI technique. In the HEARTY randomized trial,^{21,22} Sigal and colleagues²¹ reported significant reductions in total fat (%), waist circumference, and abdominal SAT, but not visceral fat, in response to aerobic, resistance, or combined AE and RE training with caloric restriction (daily energy deficit 250 kcal) in adolescents with obesity. In that study, the reductions in total fat (%), waist circumference, and abdominal SAT were similar among three exercise groups. Although they demonstrated the beneficial effects of regular exercise combined with caloric restriction on total and abdominal SAT, the influence of sex on the changes in total and abdominal AT was not reported.

Several studies in adults have demonstrated that with weight loss, men lose significantly more visceral fat than women.^{1,4,5} However, these findings^{1,4,5} are confounded by greater weight losses in men than in women with obesity. Furthermore, when comparing sex differences in body compositional changes, pretreatment values should be considered as greater initial values are associated with greater reductions in AT during weight loss.¹ Indeed, Janssen and Ross²³ have shown that after controlling for preintervention AT values, reductions in total body fat, SAT, and visceral fat are similar between men and women with obesity in response to weight loss ($\sim 10\%$ of initial body weight), which was induced by either diet alone or diet with exercise. Our study employing whole-body MRI technique is consistent with the previous findings by Janssen and Ross²³ and demonstrates in adolescents that in response to either AE or RE without caloric restriction, there are no significant sex differences in the reductions in total fat and SAT, lower body SAT, and visceral fat when initial values are taken into account. Furthermore, independent of exercise modality, we observed similar reductions in intermuscular fat between boys and girls, which is a significant correlate of insulin resistance in adolescents with obesity.²⁴ These findings provide clear evidence that regardless of exercise modality, engaging in regular exercise (180 minutes per week) alone without caloric restriction is effective in reducing total and regional fat depots in both boys and girls with obesity.

In our study, boys had significantly greater increases in total skeletal muscle, and upper body and abdominal skeletal muscle mass than girls in response to similar RE

regimen (e.g., intensity, duration, and frequency). Although the reasons for greater increases in total and regional skeletal muscle in boys are unclear, increases in growth hormone and androgen levels during puberty in boys may result in significant increases in skeletal muscle mass and muscular strength after RE. Given that increasing skeletal muscle is crucial for glucose homeostasis and energy balance, RE should be incorporated in weight management strategies to treat adolescents with obesity.

In this study, we found that the increase in $\text{VO}_{2\text{max}}$ was significantly greater in boys than in girls, independent of exercise modality. In the HERITAGE family study, Bouchard and Rankinen²⁵ reported that age, sex, race, and baseline $\text{VO}_{2\text{max}}$ contribute about 11% of the variance of $\text{VO}_{2\text{max}}$ changes in response to 20 weeks of aerobic training in adults. Our finding that there was an increase in $\text{VO}_{2\text{max}}$ after RE in boys is consistent with the findings of Weltman et al.,²⁶ who observed significant improvements in $\text{VO}_{2\text{max}}$ (19.4%) after 14 weeks of resistance training (45 minutes per session, three times per week) in prepubertal boys. However, our findings differ from Shaibi et al.¹¹ who reported no changes in $\text{VO}_{2\text{max}}$ after 16 weeks of RE in adolescent boys with obesity. The different finding could be due to differences in training volumes, participant's adherence to the protocol, and subject characteristics (black and white boys vs. Hispanic boys). For example, participants in Shaibi et al.'s study¹¹ exercised 2 days per week for 16 weeks; day 1 consisted of five different lower body exercises and isolated upper body exercises, and day 2 consisted of five different upper body exercises and isolated lower body exercises. On the contrary, our study participants performed 10 whole-body REs per day, 3 days per week for 13 weeks, and achieved high exercise adherence (99%). Clearly, further studies are needed to confirm our findings.

The strengths and limitations of this study warrant mention. By employing the gold-standard whole-body MRI technique, we examined sex differences in the changes in total fat and skeletal muscle, and regional fat and skeletal muscle in separate anatomical regions (e.g., lower body, upper body, and abdomen) in response to exercise training in adolescents. As treatment changes are often related to the baseline value, we adjusted all analyses examining treatment effects for that corresponding baseline value. However, our sample size is relatively small, which may limit our power to detect true sex differences in the changes in body fat and skeletal muscle distribution with exercise training. Our findings are also limited to black and white adolescent boys and girls with obesity. Whether our observation would remain true in other racial groups or prepubertal boys and girls is unknown. It is also unknown whether sex differences exist in the mobilization of AT in response to clinically significant weight loss in adolescents with obesity.

In summary, our study demonstrated that both AE and RE without caloric restriction are beneficial in reducing total and regional fat independent of sex, and that there

were no sex or exercise treatment differences in the changes in body weight, BMI, BMI z-score, total fat, total SAT, upper body and lower body SAT, visceral fat, or intermuscular fat in adolescents with obesity. We found that in response to RE, the increases in total, upper body, and abdominal skeletal muscle mass were significantly greater in boys than in girls. Based on these findings, we suggest that both AE and RE are similarly effective in reducing total and regional AT, independent of sex. For adolescent boys with obesity who also want to increase skeletal muscle mass, RE should be incorporated in their exercise regimen.

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Author Disclosure Statement

No competing financial interests exist.

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